Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 November 2009 has been entered.

Response to Arguments

Applicants' argue the merits of the Rejections under 35 U.S.C. §103 over claims 21, 25, 27, 31, 33, and 37 as not bring obvious due the applicants' disclosure that the detrimental impact of R-citalopram on escitalopram in racemic citalopram was neither known nor reasonably predictable, and because the claimed invention is associated with unexpected results.

Further, applicants' contend that Examiner's definition drawn to potency is improper in view of the claimed invention.

Additionally, applicants' assert the rejection of record fails to show that the administration of escitalopram alone would provide the demonstrated superior therapeutic effect as compared to racemic citalopram.

Applicants' arguments are considered but are not found persuasive because the limitation drawn to this specific distinction in view of escitalopram is no where represented in the current claim set. Absent of any clear indication in the claim set that unexpected results have occurred due to this specific distinction drawn to escitalopram as disclosed by the applicants' makes applicants' arguments moot. The Examiner interprets the claim as it appears in claim 21 to read

solely on the compound escitalopram with no provisos or alleged distinctions connected to escitalopram. The (6) claims pending for further prosecution are not commensurate with applicants' current said response of 24 November 2009.

Further, potency is the dose of drug required to produce a specific effect of given intensity as compared to a standard reference. Potency is a comparative rather than an absolute expression of drug activity. Drug potency depends on both affinity and efficacy. Thus, two agonists can be equipotent, but have different intrinsic efficacies with compensating differences in affinity.

In the way of proving comparatively the potency of escitalopram in view of the claimed invention, the applicants' are grossly deficient. Applicants' clinical study consists of (4) brief paragraphs which cite nothing in support of applicants' alleged invention. In fact, the specification is wholly deficient in showing the bare minimum with regard to their claim of superior potency. By virtue of applicants' definition of potency on page 3 in the 1st paragraph drawn to a *comparison* with a different agent, applicants' invention is not proper in view of addressing the potency of escitalopram as a first order of issue. The clinical studies only compare escitalopram to placebo which cannot be any drug related to escitalopram according to the conventional use of a study. Applicants' have not shown in the clinical studies the clear delineation between the R-enantiomer and the S-enantiomer as far as claimed potency.

Lastly, applicants' assert that the rejection of record fails to show the administration of escitalopram alone would provide the demonstrated superior therapeutic effect as compared to racemic citalopram. However in response, the burden remains with applicants to

clearly delineate this claimed distinction drawn to escitalopram in the specification and current claims at issue.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 21, 25, 27, 31, 33, and 37 are pending further prosecution on the merits.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21, 25, 27, 31, 33, and 37 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Patris M, et al. ("Citalopram versus fluoxetine; a double-blind, controlled, multicentre, phase III trial in patients with unipolar major depression treated in general practice," 1996 International Clin Psychopharm 11: 129-136), in view of Boegesoe et al. (US Pat. 4,943,590), and further in view of Maisey et al. (US Pat. 4, 079,135).

Patris et al. teach the administration of citalopram in the treatment of patients with major depression (abstract). Patients had a score of 30 on the MADRS at the beginning of the 8-week treatment period (see Fig. 1 p. 132). The reference teaches assessment of the efficacy of treatment by measuring the MADRS score as well as by the CGI severity and improvement scale (see pp. 130 and 134).

Patris et al. do not teach escitalopram (the S-enantiomer) specifically.

Boegesoe et al. teach that antidepressant drug citalopram has two enantiomers, (+)-citalopram (which is escitalopram) and (-)-citalopram, and that the entire 5-HT uptake inhibition activity resides in the (+) enantiomer (i.e. escitalopram) (see: abstract; col. 1, lines 1-28; col. 2, lines 9+). The reference also teaches separation of the two enantiomers to yield pure citalopram enantiomers (see col. 2, lines 51 - col. 7, line 25). The reference teaches, "a method for alleviating depression in a living animal body subject thereto" by administering an effective amount of the compound or pharmaceutically acceptable salts (which is escitalopram), at dosages ranging from 0.10-100 mg and preferably 5-50 mg daily (overlapping the dosage of current claim 25). (See: abstract; col. 8 Table 1; col. 8, lines 55-66; claims 1-2 & 7-12).

While Boegesoe et al. teach pharmaceutically acceptable salts; the reference does not teach oxalate salts specifically.

The deficiency of Boegesoe is resolved by the teachings of Maisey.

Maisey teaches a method of relieving or preventing depression in warm-blooded animals, including man, which comprises administering thereto an anti-depressant effective amount of a compound of the formula: ##STR36## wherein R.sup.1 is

hydrogen or halogen, or alkyl or alkoxy of 1 to 3 carbons; A is a radical of the formula: ##STR37## wherein R.sup.2 and R.sup.3, which may be the same or different, are hydrogen or alkyl of 1 to 3 carbons and B is oxygen; and the non-toxic, pharmaceutically-acceptable acid-addition salts thereof in association with a major amount of a non-toxic, pharmaceutically-acceptable diluent or carrier (col. 16, l. 42)

Maisey teaches an embodiment which suggests and supports that conversion to a crystalline oxalate salt is a standard procedure (col. 9, l/s 56 and 57).

Maisey does not teach escitalopram but it does teach an agent indicated for treating depression.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art to use the oxalate or crystalline oxalates salt of escitalopram in the instantly claimed method of treating severe depression, having been taught by the prior art that it is known to make oxalate and crystalline oxalate salts of a racemic compound to obtain the (S) isoform and motivated by the desired to obtain the (S)/(+) isoform salt of citalopram (i.e. escitalopram), which is known to be the racemate wherein the pharmaceutical antidepressant activity resides. Patris establishes the fact that within citalopram is contained the (S)-enantiomer which is escitalopram. Boegesoe definitively teaches the subject matter of the claimed invention, because Boegesoe addresses and encompasses the bioactive agent and dosage parameters of the claimed invention. Further, based on the teachings of Maisey the conversion of a compound indicated for depression to a more pure compound is disclosed as a standard procedure. As mentioned before, the limitations

of the instant claims drawn to a salt species are functional language and hold no patentable weight in view of claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

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